

II. REMARKS

Preliminary Remarks

Claims 29-34 and 36-61 are currently pending in this application. Claims 56-58 are allowed. Accordingly, claims 29-34, 36-55, and 59-61 are at issue.

The applicants have amended claim 29 to be directed to a process for the preparation and improvement of a pantothenic acid-producing microorganism comprising amplifying a panE gene in said microorganism and then incubating said microorganism under conditions suitable for the production of the panE gene product, ketopantoate reductase wherein the microorganism is selected from the group consisting of *Escherichia* and *Saccharomyces*. Support for the amendment can be found throughout the specification, for example, in Examples 5, 6, 14, 15, and 17 and page 8, line 13 to page 9, line 19.

Claims 37, 38, and 61, which ultimately depend upon claim 29, have also been amended to more succinctly define the microorganisms involved in the applicants' claimed process.

Claims 42 and 43 have been amended in order to include the gene ilvC that encodes for isomeroreductase as an additional gene product involved in the metabolic path of pantothenic formation. Support can be found throughout the specification, for example, at page 2, line 27 to page 3, line 2.

Claims 48, 49, and 51-53 have been cancelled without prejudice. Claims 50, and 54 have been amended to be directed to specific species of microorganisms selected from the group consisting of *Escherichia*, and *Saccharomyces* that can be used in the process of claim 29. Support can be found throughout the specification, for example, originally filed claims 49-54, and Examples 6, 14, and 17.

The applicants believe that no new matter has been added as a result of these amendments and respectfully request reconsideration and allowance of the present application.

Patentability Remarks:

Rejection Pursuant to 35 U.S.C. §112, first paragraph, written description

The examiner has rejected claims 29-34, 36-55, and 59-62 under 35 U.S.C. §112, first paragraph, for allegedly lacking written description. Specifically, the examiner alleged the rejected claims encompass an enormously broad genus of genes encoding ketopantoate reductase activity from any different microorganism, which may also include untranslated regions normally associated with the gene encoding ketopantoate reductase activity. The

examiner further alleged the specification does not provide the nucleic acid sequences for either of the two exemplified embodiments (*E. coli* (panE gene) and *S. cerevisiae* (YHR063c)), although biological deposits have been made which satisfy the written description requirement for the exemplified embodiments. The examiner further asserted no description has been provided for the untranslated region associated with either gene and the specification does not provide a basis for one of skill in the art to envision additional embodiments aside from those exemplified from *E. coli* and *S. cerevisiae*. The examiner further alleged that the prior art (Frodyma *et al.*, *J. of Biol. Chem.* 273:5572-5576 (1998)) does not offset the deficiencies of the instant specification regarding reliably envisioning what additional coding sequences encoding a ketopantoate reductase activity might look like (much less what the non-coding regions of such genes might comprise). The examiner concluded that given the broad genus of potential ketopantoate reductase genes embraced by the rejected claims, and given the lack of any basis for one of skill in the art to reliably predict what additional genes encoding ketopantoate reductase activity might look like, one of skill in the art would not be able to envision a sufficient number of ketopantoate genes to describe the broadly claimed genus of such genes that are to be amplified in the instant claims.

Solely for the purpose of expediting prosecution, and without prejudice to the applicants' right to seek broader claims in a continuing application, the applicants have amended claim 1 to be directed to a process for preparation and improvement of a pantothenic acid-producing microorganism comprising amplifying a panE gene in said microorganism and then incubating said microorganism under conditions suitable for the production of the panE gene product, ketopantoate reductase wherein the microorganism is selected from the group consisting of *Escherichia* and *Saccharomyces*. The examiner acknowledged that the applicants described the amplification and expression of the ketopantoate reductase gene from *E. coli* and *S. cerevisiae*. (See Office Action, page 3, first full paragraph, line 1). In addition, claims 51-53 have been cancelled without prejudice.

In view of the foregoing amendments and remarks, the applicants respectfully submit that the rejection of claim 29 and dependent claims 30-34, 36-55, and 59-61 pursuant to 35 U.S.C. § 112, first paragraph, for lack of written description, is moot and should be withdrawn.

Rejection Pursuant to 35 U.S.C. §102(b), anticipation

On page 5 of the official action, the examiner has rejected claims 29, 30, 33, 34, 36, 48-50, and 61 under 35 U.S.C. §102(b) as being anticipated by Frodyma et al., J. of Biol. Chem. 273:5572-5576 (1998) (hereafter Frodyma).

Specifically, the examiner alleged that in lieu of the specification's definition of the term "amplification," *i.e.*, and the phrase "is intended to mean an increase in the intracellular activity of one or more enzymes which are coded for by the corresponding DNA by increasing the number of copies of the gene(s), using a potent promoter or a gene which codes for a **corresponding enzyme** having a high specific activity, and optionally combining the different measures" (page 3, lines 3-7) (emphasis added), the gene taught by Frodyma *et al.* would necessarily be considered by the skilled artisan as encoding a **corresponding enzyme** to that encoded by a panE gene because both enzymes comprise the same ketopantoate reductase activity. The examiner concluded that one of skill in the art could reasonably conclude that the apbA gene characterized by Frodyma *et al.* is a panE gene due to its high ketopantoate reductase specific activity. The applicants respectfully request reconsideration and withdrawal of the rejection in light of the amendments and remarks.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." See *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628 (Fed. Cir. 1987).

The applicants submit that Frodyma *et al.* did not disclose each and every element of the applicants' invention, as amended and claimed herein. Specifically, the applicants contend that Frodyma *et al.* do not, either expressly or inherently, teach a process for the preparation and improvement of a pantothenic acid-producing microorganism comprising amplifying a gene in said microorganism and then incubating said microorganism under conditions suitable for the production of the panE gene product, ketopantoate reductase **wherein the microorganism is selected from the group consisting of *Escherichia* and *Saccharomyces*.**

In contrast, Frodyma *et al.* teach the cloning and expression of the apbA gene from *S. typhimurium* in *E.coli* and the purification of its gene product, ketopantoate reductase. The examiner acknowledges that applicants teach the concept of amplifying the panE sequences to increase production of pantothenic acid in a microorganism appears to be novel in the art (page 4 of the official action). As discussed above, the applicants teach the overexpression of panE in numerous strains of *E.coli* and YHR063c in numerous strains of *S. cerevisiae* and provide sufficient description of finding and for acquiring this gene in *Escherichia* and

Elischweski et al. -- Appl. No. 09/680,310

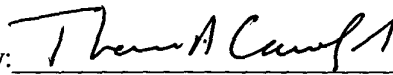
Saccharomyes. Dependent claims 30, 33, 34, 36, 48-50 and 61 are submitted to be patentable for at least the same reasons as independent claim 29, as well as features that each of these claims directs. Accordingly, the applicants respectfully request that the rejection be withdrawn.

III. CONCLUSION

In view of the foregoing, the claims are still believed to be in form for allowance, and such action is hereby solicited. If any point remains in issue which the examiner feels may be best resolved through a personal or telephone interview, the examiner is **strongly urged** to contact the undersigned at the telephone number listed below.

Respectfully submitted,

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